Remarks

The Office action mailed July 28, 2005, has been reviewed and carefully considered. Claims 1, 16, 17, 53, and 88 have been amended. Entry of these amendments is respectfully requested.

35 U.S.C. §112 Rejection

Claims 32-42 have been rejected under 35 U.S.C. §112, second paragraph, for alleged indefiniteness because "the method steps do not require any genetic or expression analysis" (see page 3 of the Office action). However, a review of claim 32 reveals that the claim language does, in fact, refer to detecting gene expression. Claim 32, lines 3-4 include the phrase "with a nucleic acid array that detects which genes are abnormally *expressed* in the biological specimen" (emphasis added). Claim 32, line 7 includes the phrase "to detect which genes are abnormally *expressed* in the biological specimens" (emphasis added). Accordingly, the pending 35 U.S.C. §112, second paragraph, rejection of claims 32-42 should be reconsidered and withdrawn.

35 U.S.C. §102 Rejections

Claims 1-2, 4-9, 11-12, 14, 16-20, 29-30, 49, 53-61, 70, 87-89 and 91-92 have been rejected under 35 U.S.C. §102 over Enghardt et al. This rejection is traversed for the reasons presented below and in applicants' earlier responses.

Applicants continue to maintain that there is no teaching in Enghardt et al. of subjecting successive copies or sections of the array to first and second assays, respectively, that are

different to determine if there are correlations between the results of the assays for an assigned specimen location. There is no explicit statement in Enghardt et al. that serial sections (e.g., section #1 and section #2) of the multitissue control block (MTCB) are subjected respectively to different antibody assays (e.g., antibody assay #1 and antibody assay #2) and the results of each assay are compared against each other for a specific specimen or sample (e.g., sample at coordinate [1,1] of section #1 versus sample at coordinate [1,1] of section #2). Indeed, Enghardt et al. makes no mention of utilizing an x-y coordinate position system in order to perform the analysis described therein. Independent claims 1, 16, 53 and 88 have now been amended to specify an x-y coordinate position system to further distinguish over Enghardt et al.

The Office action on page 4 asserts that "Enghardt et al. further teach the method compares first array (control) to a second array wherein using different assays i.e. the control array comprises the preliminary sections tested with hematoxylin and eosin Y (page 53, right column, 7th full paragraph, Fig. 2) and the second array is assayed for antibody staining to the test array." However, a careful review of Enghardt et al. reveals no mention of comparing and correlating the results of the hematoxylin and eosin Y staining with the antibody staining results. The hematoxylin and eosin Y staining was used "to ascertain the complete demonstration of all tissue samples" (Enghardt et al., page 53, second column, 7th full paragraph). In other words, this staining was performed simply to confirm that the tissue block was made correctly (e.g., there were no air pockets).

Applicants' reply mailed May 9, 2005, also pointed out that Enghardt et al. only specifically mentions comprising internally within a single slide between the results for an arrayed multitissue control block versus the results for a patient sample. For example, Enghardt et al. states on page 54, column 1, that "[w]hen placed on the same slide as the patient sample,

the multitissue control serves as a convenient record for validation of reactivity." Enghardt et al. further states on page 54, column 2, that "[t]he small size of the core pattern allows the patient sample to be placed on the same slide, thus facilitating interpretation and quality control for each specimen."

In reply to applicants' argument regarding Enghardt et al.'s internal comparison within a singe slide, the Office action on page 9 notes that "the claims are not limited to different slides." In order to further prosecution, independent claims 1, 16, 53, and 88 have now been amended to specify that each array copy, array cross-section, or matrix copy is placed on an individual separate support (e.g., a slide). The comparison and correlation contemplated by the presently claimed methods involves comparing the results from a first array, cross-section or matrix disposed on a first support to the results from a second array, cross-section or matrix disposed on a second support. Enghardt et al. does not teach comparing the results from a first slide to the results of a second slide.

The Office action on page 9 further states that "Enghardt does teach multiple slides for analysis of 12 anitbodies (page 53, right column, 8th paragraph-end of page)." The cited passage from Enghardt et al. simply discloses that sections from the multitissue control block were placed on slides. There is nothing in the cited passage suggesting that the results from a first slide are compared to the results of a second slide.

In summary, Enghardt et al. fails to disclose all the features of the rejected claims. Accordingly, the 35 U.S.C. §102 rejection over Enghardt et al. must be withdrawn.

Claims 32-42 have been rejected under 35 U.S.C. §102(e) over An et al. This rejection is traversed because An et al. does not disclose all the features presently recited in claim 32.

Claim 32 employs a nucleic acid array, wherein the nucleic acid array comprises an arrangement of nucleic acid in assigned locations on a matrix. The passage from An et al. cited in the Office action as disclosing a nucleic acid array does not, in fact, disclose such an array. An et al. discloses plating a cDNA library on agarose plates. Subsequently, *"[i]ndividual* colonies are transferred to nylon or nitro-cellulose membranes and the EST probes are hybridized to complementary sequences on the membranes" (column 3, lines 39-41) (emphasis added). There is no teaching in An et al. that the individual colonies are arranged in assigned locations on the membranes.

In addition, claim 32 includes "screening multiple biological specimens in a biological specimen *microarray.*" The passage from An et al. cited in the Office action as disclosing this feature does not, in fact, disclose screening a biological specimen microarray. Column 4 of An et al. describes a kit that includes probes for binding to markers in a Northern blot assay. A Northern blot assay is not a biological specimen microarray.

35 U.S.C. §103 Rejections

Dependent claims 22, 46-48 and 98-100 have been rejected for obviousness in view of Enghardt et al. However, as explained above, the teaching in Enghardt et al. is fatally deficient with respect to the base independent claims. Thus, an obviousness rejection over Enghardt et al. alone also must be fatally flawed.

Dependent claims 24-28 and 114-123 have been rejected for obviousness in view of Enghardt et al. combined with An et al. The Office action recognizes that Enghardt et al. does

not disclose the use of a nucleic acid microarray. An et al. is relied upon for supplying this absent feature, but An et al. does not actually disclose a nucleic acid microarray as explained above in connection with the lack of novelty rejection. The combination of Enghardt et al. and An et al. would not have resulted in the claimed invention. Hence, the pending obviousness rejection must be withdrawn.

Dependent claims 31, 50-52, 62-63, 68-69, 71-78 and 86 have been rejected for obviousness over Enghardt et al. combined with Stapleton et al. Stapleton et al. is relied upon for allegedly disclosing the analysis of certain specific types of tissue. However, there is nothing in Stapleton et al. that cures the above-discussed deficiencies in Enghardt et al. Thus, the pending obviousness rejection of Enghardt et al. combined with Stapleton et al. must be withdrawn.

Dependent claims 66 and 67 have rejected for obviousness over Enghardt et al. combined with Stapleton et al. and An et al. However, as explained above, neither Stapleton et al. nor An et al. cures the fatal deficiencies in Enghardt et al. with respect to the base independent claims.

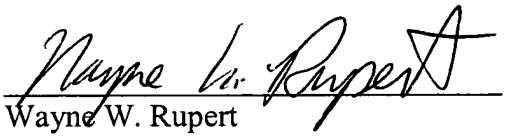
Interview Summary

Applicants hereby agree that the Interview Summary form prepared and mailed by the examiner on January 13, 2006, accurately reflects the discussion between the undersigned and the examiner.

It is respectfully submitted that the present application is in condition for allowance. Should there be any questions regarding this application, examiner Forman is invited to contact the undersigned attorney at the telephone number shown below.

Respectfully submitted,

KLARQUIST SPARKMAN, LLP

By 
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